Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 28578P WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/008230	International filing date (*day/month/year*) 25 July 2003 (25.07.2003)	Priority date (*day/month/year*) 25 July 2002 (25.07.2002)
International Patent Classification (IPC) or national classification and IPC C07D 295/205		
Applicant WILEX AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 19 September 2003 (19.09.2003)	Date of completion of this report 07 October 2004 (07.10.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/008230

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:
pages 1-9, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:
pages 1-5, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the drawings:
pages 1/4-4/4, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1 (in part), 3, 4, 5 (in part)

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1 (in part), 3, 4, 5 (in part).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box III.

No preliminary examination is carried out in respect of subjects which have not been searched (see the international search report). The present examination is therefore restricted to the first invention as specified on supplementary sheet PCT/ISA/210 of the international search report.

V. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1 (in part), 2, 5 (in part)	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1 (in part), 2, 5 (in part)	NO
Industrial applicability (IA)	Claims	1 (in part), 2, 5 (in part)	YES
	Claims		NO

2. Citations and explanations

1. Reference is made to the following documents:

D1: WO-A-9208709

D2: *Bioorg. Med. Chem. Letters*, **1999**, *9*(17), 2483-2486

D3: *Bioorg. Med. Chem. Letters*, **1999**, *9*(21), 3147-3152

2. The subject matter of claim 1 lacks novelty (PCT Article 33(2)):

2.1 D1 discloses (see example 1) a method for producing 3-amidino phenylalanine derivatives, in which method 3-cyanobenzyl bromide is reacted with an N-protected amino malonic acid diester (acetamido malonic acid diethylester) to produce 3-cyanophenylalanine (example 1, (1) and (2)).

The method as per D1 differs from the present method in that the N-protected 3-cyanophenylalanine is not isolated.

2.2 The method disclosed in D2 differs from the present method by virtue of the end product.

2.3 D3 does not describe the production of 3-cyanophenylalanine.

3. The solution proposed in claim 1 of the present application cannot be considered inventive (PCT Article 33(3)) for the following reasons:

The present application is considered to address the problem of developing an alternative method for producing 3-amidino phenylalanine derivatives.

The present method differs from the method as D1, which is regarded as the closest prior art, only in that the decarboxylation and the removal of the protective groups take place in separate steps. Since the conditions for decarboxylation and separation of protective groups are generally known in the art (see, for example, document D2), the implementation of these measures would be an obvious procedure to a person skilled in the art for solving the stated problem.